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ORIGINAL ARTICLE

Comparative study between black blood T2* and conventional bright GRE sequences in assessment of myocardial iron concentration

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Abstract *Purpose:* To compare the efficacy and reproducibility of black blood T2* to the conventional bright blood sequence in the assessment of myocardial iron concentration.
Materials and methods: We performed both conventional bright blood and black blood MRI T2* sequences in 50 thalassemia major patients, the results were statistically analyzed to assess the correlation of techniques, study reproducibility and interobserver agreement.
Results: Cardiac T2* values ranged from 2.39 to 47.9 ms using bright blood sequence and 2.07 to 46.81 using the black blood sequence. There was positive significant correlation of both sequences in all patients. However the black blood technique was superior to bright blood technique as regards the study reproducibility ($R2^*$1.9 ± versus 2.4 ± 14.7 $p < 0.001$) in addition to the better inter-observer agreement of black blood technique compared to the bright blood technique (3.2 ± 1.2 versus 8.3 ± 2.4 $p < 0.001$).
Conclusions: Black blood T2* technique provides clearly defined septal borders, avoids bright blood signal contamination of the myocardium, has superior study reproducibility and inter-observer agreement which favors this technique in the assessment of iron myocardial concentration.

1. Introduction

Patients of thalassemia major on regular blood transfusions suffer from inevitable accumulation of iron in tissues of the heart, liver, and endocrine systems. Myocardial iron deposition resulting in cardiac failure and death at a young age. Early detection and assessment of myocardial iron is crucial to

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evaluate the risk of cardiac complications and tailoring appropriate iron chelating treatment (1).

Despite the fact that transfusions improve health and survival, however the consequent tissue iron deposition causes organ damage in the long term. Patients treated with regular blood transfusions usually die early from cardiac failure secondary to myocardial siderosis (2).

Cardiomyopathy can be treated if intensive iron chelation treatment is initiated properly (3), but diagnosis is often delayed by the concealed cardiac iron deposition and the late development of symptoms, and echocardiographic abnormalities (4). Once heart failure develops, the prognosis is usually poor with abrupt deterioration and death, even with intensive chelation therapy (5).

Early diagnosis and measurement of myocardial iron deposition would allow proper management and help to reduce mortality from this reversible cardiomyopathy; however, endomyocardial biopsy is inaccurate for measuring myocardial iron because of high rate of sampling error with very small biopsy samples (6,15).

The need for an alternative noninvasive measurement of myocardial iron led to the development of an optimized cardiac $T2^*$ magnetic resonance (MR) technique (7).

Intracellular iron particles deposition causes shortening of the MR relaxation parameter $T2^*$ with increase in its reciprocal, $R2^*$ due to microscopic magnetic field in-homogeneity.

$T2^*$ decay is measured by gradient echo CMR, and iron overload is diagnosed when the values are less than 20 ms (8). Recently, single breath-hold sequence was evolved with shorter scan time, better image registration between images, and excellent reported reproducibility (9). This technique has become the standard for myocardial iron concentration assessment and has also proved value in the assessment of chelation regimens (10).

The white blood technique, however, has some undesirable characteristics including poor contrast between blood pool and myocardial margins, motion artifacts and blood flow compromising measurement accuracy. Recently, a black blood' double inversion recovery sequence which suppresses the blood signal, has reported a preliminary good reproducibility compared to the white blood $T2^*$ imaging technique (11).

2. Objectives

Our study aimed to compare the efficacy and the technical reproducibility of black blood $T2^*$ and the conventional bright blood sequence in the assessment of myocardial iron concentration.

3. Patients and methods

A prospective two-year study of 50 patients on regular blood transfusion, referred for MRI assessment of cardiac siderosis has undergone an imaging protocol which includes measurement of cardiac $T2^*$ using pulse sequences without and with a blood suppression prepulse to evaluate interstudy reproducibility.

All the patients were known TM and were on regular blood transfusion for more than 18 months. Between the age range 8 and 41 years (mean 27) 56% were male.

17 patients (34%) showed cardiac siderosis ($T2^* < 20$ ms).

Our patients were examined by a 1.5 T scanner (Siemens Espree, Erlangen, Germany) with a 8 channel phased array cardiac coil and ECG gating.

Three mid-ventricular short axis scans with 6 mm slice thickness were obtained. For bright blood acquisition, we used a multi echo gradient sequence (matrix 128×256 pixels, field of view 40 cm, and flip angle 20°). The short axis images were taken with a single breath-hold (8–12 s) at 8 different echo times ranged from 2.54 to 17.90 ms at 2 ms increments. Images of white blood technique were scanned immediately after the R-wave, while for black blood acquisition, we apply a double inversion recovery pulse on the R-wave with prolonged inversion time to diastole, that developing 8 increasing echo time sets of images (12).

We analyze our images using Thalassemia CMR tools (Cardiovascular Imaging Solutions, London, UK). Our ROI full thickness section included the ventricular septum but avoiding the blood pool cavity and cardiac vessels (13,14).

$T2^*$ was acquired using an exponential curve fit, $SI = SI0 \cdot \exp(TE/T2^*)$, and the back ground noise in delayed echo times was detected in bright blood technique only, and was removed using the truncation method for better curve fit. The image quality and the presence of artifacts were assessed in all sequences.

3.1. Statistical methods

Data were statistically analyzed using SPSS (Statistical Package for Social Sciences version 20.0). First, the excel file was imported then full labeling of all variables and their values were performed with exploration of data for any odd or abnormal values before performing the preliminary analysis.

Line graph was utilized to present the correlation between bright blood and black blood techniques.

We apply Kaba test in the analysis and the assessment of image quality and a p value of <0.05 was considered significant.

4. Results

All 50 patients included in this study had thalassemia major anemia and were receiving regular blood transfusion. Between the age range 8 and 41, means SD 23.38 ± 8.8, 28 were males and 22 females.

Table 1 shows characteristics of the patients ($N = 50$), showing 56% of the patients aged from 20 to 39 years with Mean + SD (23.38 ± 8.8 years). Most of the patients were males.

Table 1 Age and sex distribution of 50 patients.

Characteristics	Patient	
	$N = 50$	%
Gender		
Male	28	56
Female	22	44
Mean ± ST. deviation		
Age		
Range	8–41	
Mean ± ST. deviation	23.38 + 8.8	

4.1. T2* myocardial iron concentration results of black blood and bright conventional sequences

Out of 50 patients 33 were normal, while 17 showed varying degree of myocardial iron concentration: 6 were light, 6 moderate while 5 showed severe iron myocardial concentration. Table 2 shows that the majority of our patients (33%) were non cardiac siderosis and only (17%) had severe degree of iron deposition.

The values of cardiac T2* ranged from 2.39–47.9 ms as measured with bright blood acquisition and 2.07–46.81 ms using the black blood sequence.

We reported no significant difference between the mean cardiac T2* values for all 50 patients using both the black blood and the conventional bright blood sequences (30.46 ms versus 30.12 ms; $p = 0.26$).

Table 2 Distribution of disease severity among study population.

Grade (severity)	Patients	
	$N = 50$	%
Normal	33	66
Light	6	12
Moderate	6	12
Severe	5	10

Table 3 Cardiac T2* values measured by bright and black blood techniques.

Myocardial iron concentration (g/ms)	Bright blood	Black blood
Normal	29.59–47.95	30.22–46.81
Light	16.30–18.72	16.48–18.11
Moderate	12.45–13.88	12.04–12.67
Severe	2.39–4.56	2.07–4.21
Mean ± SD	30.12 + 14.7	30.46 + 1.47
R	0.99	
p value	0.000[a]	

[a] High significance.

Table 3 and Fig. 1 show the positive significant correlation between bright and black blood techniques. p value = 0.000.

The black blood and the white blood acquisitions were also not significant for the iron loaded ($N = 17$, $p = 0.31$) and non-iron loaded ($N = 33$, $p = 0.081$) subgroups.

The black blood technique was superior to the bright blood technique as regards the study reproducibility (R2*1.9 ± 2.07 versus 2.4 ± 14.7) in addition to the better inter-observer agreement concerning the black blood technique compared to the bright blood technique (3.2 ± 1.2 versus 8.3 ± 16.4).

4.2. Blood suppression and image quality

Images acquired from midventricular septum using bright- and black-blood sequences (Fig. 2) show the better delineation of myocardial septum borders with less artifacts in black blood T2* images. Blood signal seems contaminating the myocardium in the bright blood image while the myocardium in the black-blood images is homogeneous.

The analysis of the T2* decay curve and the black blood T2* sequence showed an improved curve fit compared to the conventional bright blood sequence (Fig. 3).

In severe iron loaded hearts, the fast signal decay causes the curve to plateau in delayed echo times. Bright blood technique (top image) shows the lower points below the level of background noise (red crosses) causing improper curve fit, so we used the truncation method in the conventional bright blood technique (R2 = 0.9983 with truncation). However, the black blood technique reduced the background noise with better curve fit through the eight gradual increasing echo times, without any truncation (R2 = 0.9996) and this diminishes the analysis errors.

5. Discussion

Iron-overload due to recurrent blood transfusions leading to heart failure related cardiomyopathy is considered the most frequent cause of mortality in patients with thalassemia major. Iron overload is related to repeated blood transfusion, with each unit of blood containing 200–250 mg of elemental iron, along with excessive gastrointestinal adsorption. Transfusional iron is deposited in the reticuloendothelial system (RES); when

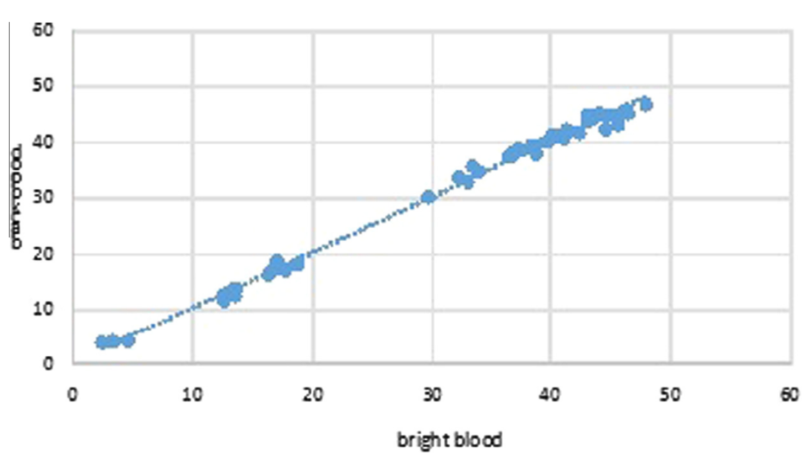

Fig. 1 Shows positive significant correlation between bright and black blood techniques.

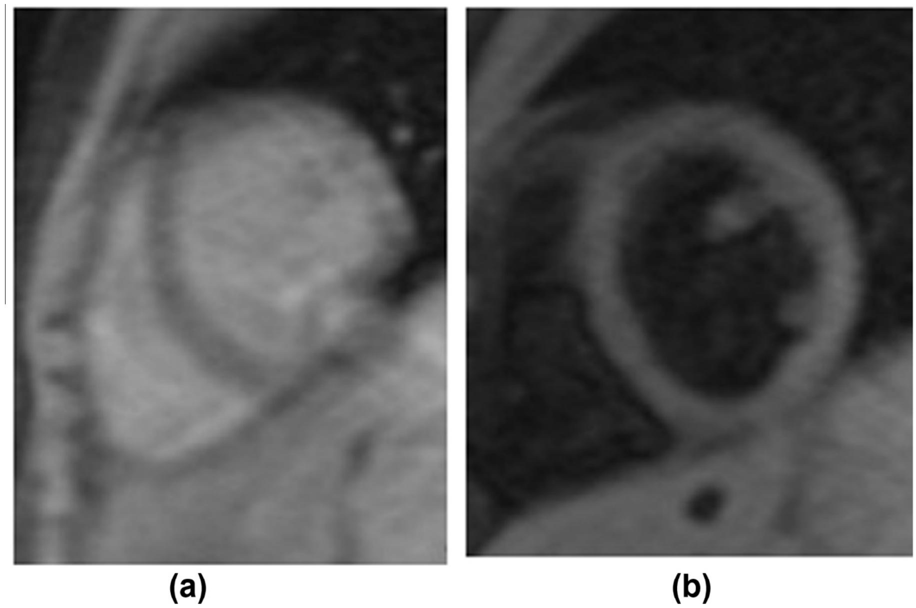

Fig. 2 (a) Bright blood and (b) black blood techniques of short axis midventricular images obtained from the same thalassemia patient showing the superior image quality and clear septal margins of the black-blood technique.

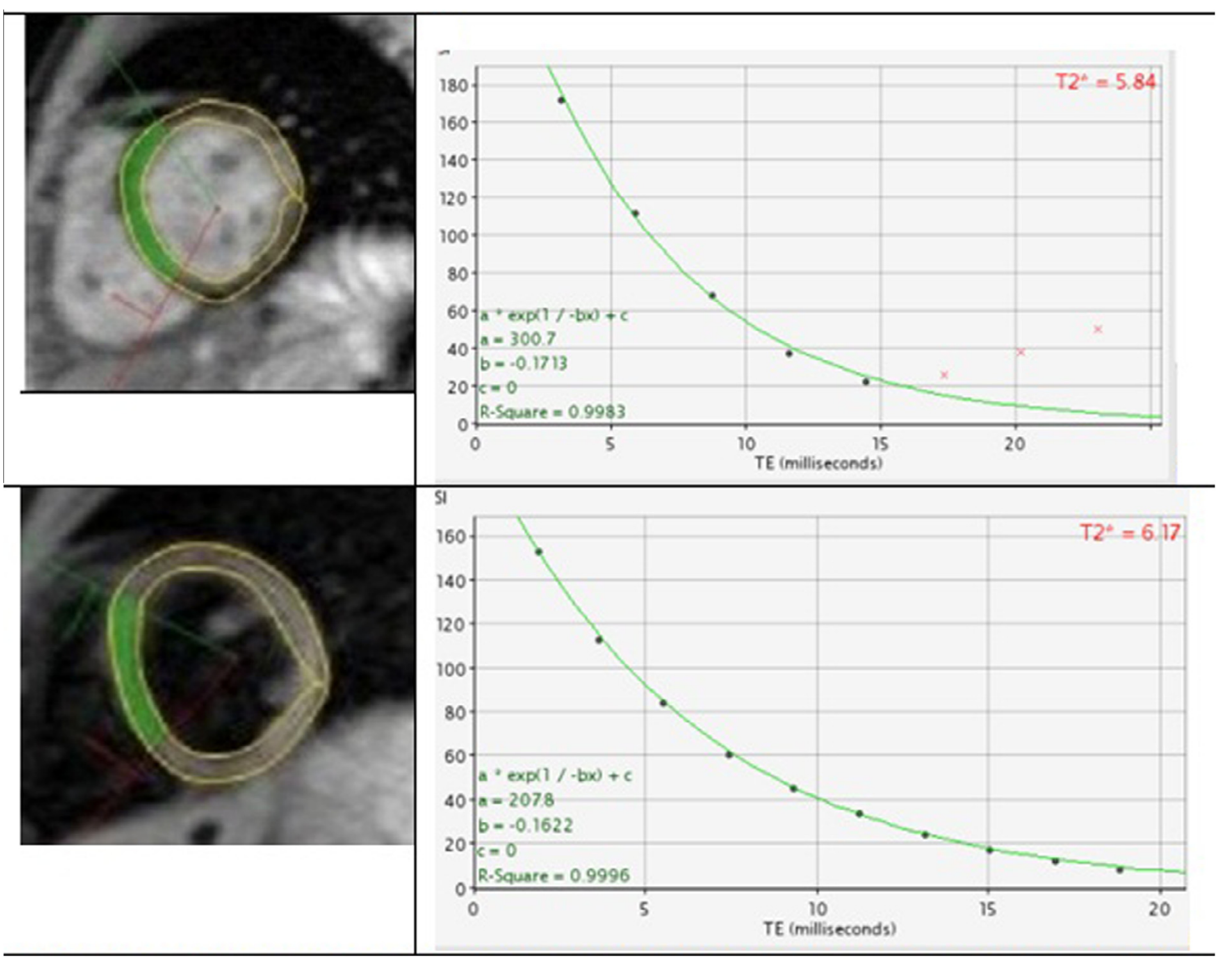

Fig. 3 Plateau curve in heavily iron loaded heart with rapid decay in the longer echo times. The top image shows the points that fall below background noise level are removed to improve curve fit (red crosses) using the truncation method for the black blood acquisition, and in lower image the background noise is reduced and thus the curve fit is complete for the full range of echo times without truncation which reduces analysis errors.

the stores of the RES are saturated, iron deposition starts to accumulate in parenchymal tissues of the endocrine glands, hepatocytes and myocardium (16,17).

Cardiac MR studies have proved that some thalassemia major patients have a heterogeneous iron deposition pattern in the myocardium as measured by in vivo T2*, although with more and severe cases of iron deposition the heterogeneity begins to diminish (18).

Myocardial T2* in vivo, however, may be confounded by a number of factors, including magnetic susceptibility artifact and measurement error. So in view of these problems, it has been recommended that T2* measurement should be restricted to a full-thickness septal ROI, with highly delineative midseptum R2* measurement (19).

Myocardial T2* and functional CMR imaging, are considered the gold standard for assessment of cardiac iron loading (20). With continuing advances of MRI technology, main field non-uniformity is mainly patient-induced and the T2* is subject to localized susceptibility artifacts (21,22). Fortunately, the susceptibility artifacts can be minimized by detaining the measured ROI to the septum, and subsequently, this technique has demonstrated good reproducibility (23–25) and lately, has been further optimized in terms of trigger delay, echo-spacing, acquisition window and other parameters (26).

A more recent advance was the inclusion of black blood preparation, which provides suppressed blood signal with clearly defined borders, less motion artifacts leading to superior reproducibility and improved interobserver agreement compared to the conventional bright blood GRE sequence (27).

In this study we included 50 TM patients on regular blood transfusion, where 17 had varying degree of cardiac siderosis while 33 were normal as measured with the conventional bright blood and suppression black blood sequences.

Our study objective was to assess the efficacy and reproducibility of black blood IR technique compared to the conventional bright blood GRE sequence in the assessment of cardiac iron concentration.

Our results showed positive significant correlation between the two techniques, with p value 0.000, in agreement with Ou et al. (28), who stated that, the use of a blood suppression prepulse black blood technique had little effect on the calculated cardiac R2*.

We reported superior study reproducibility of black blood T2* imaging in all 50 patients (R2*1.9 $\pm$ 2.07 versus 2.4 $\pm$ 14.7) and in the agreement of the inter-observer variability (3.2 $\pm$ 1.2 versus 8.3 $\pm$ 16.4). Similar results were reported by Smith et al. (29), who found a significant coefficient improvement (three folds) in intra and inter-observer variability with better inter-study reproducibility for black blood T2* imaging compared to the conventional white blood sequence.

Using conventional bright blood sequence, resulting in low signal contrast with difficulty in defining myocardium borders, hence, the blood contamination will be included in the decay curve which increases the possibility of errors in T2* measurement. Misregistration of the high signal blood pool artifacts which can be superimposed on the ROI can also increase the rate of errors.

Using the double inversion recovery black blood technique with better delineation of the myocardial borders, and reducing the noise artifacts will improve the accuracy of T2* measurement (29).

Our results showed better image quality, less artifacts and better delineation of myocardium septum, which improved decay curve analysis and reduced the requirement for truncation method in heavily loaded hearts using the black blood T2* technique, in consistent with Taigang H et al. (30) who believed that the black-blood T2* technique improved potential partial volume errors, reduced artifacts and simplified the data analysis for clinicians and therefore be less sensitive to observer training errors.

6. Conclusion

Black-blood T2* sequence has improved the assessment of myocardial iron concentration, by providing high contrast images, better myocardial border definition, reducing blood signal contamination from the myocardium and less images artifacts. We support the use of blood suppression prepulse for measurement of cardiac T2* based on its superior study reproducibility and interobserver agreement.

Conflict of interest

The authors declare that there are no conflict of interests.

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